What Is Claimed Is:

1. A method of producing a linear double stranded DNA expression vector containing a 5' terminal promoter controlling the expression of V_H and V_L polypeptides from respective V_H- and V_L-coding genes, said V_H and V_L polypeptides being capable of forming a heterodimeric receptor of predetermined specificity, which method comprises:

(a) isolating a first diverse population of V_H-coding genes containing a gene coding for said first V_H polypeptide, said first population being constituted by linear double stranded DNA molecules defining a restriction site recognized by an endonuclease, said restriction site located 5' terminal to said genes but 3' terminal to a promoter controlling the expression of said V_H-coding genes;

(b) isolating a second diverse population of V_L-coding genes containing a gene coding for said V_L polypeptide, said second population being constituted by linear double stranded DNA molecules defining said restriction site, said restriction site located 3' terminal to said V_L-coding genes, said V_L-coding genes located 3' terminal to a promoter controlling the expression of said V_L-coding genes;

(c) cleaving said double stranded DNA molecules while present in said populations with said endonuclease to produce restriction fragments having a cohesive terminus and either one of said V_H-coding genes or one of said V_L-coding genes; and

(d) randomly ligating said restriction fragments one to another via said cohesive terminus of each to produce a diverse population of double stranded linear DNA expression vectors having one of said V_H-coding genes and one of said V_L-coding genes in tandem on the same DNA strand and under the control of a single promoter;

(e) isolating from said diverse population of double stranded DNA expression vectors a vector capable of expressing said heterodimeric receptor of predetermined specificity.

2. The method of Claim 1 wherein said V_H-coding genes are V_H-coding DNA homologs and said isolating comprises:

(a) subjecting a V_H-coding gene repertoire to a first primer extension reaction utilizing a first polynucleotide synthesis primer capable of initiating said first reaction by hybridizing to a nucleotide sequence conserved with said repertoire, thereby producing a plurality of different V_H-coding DNA homolog complements, and subjecting said compliments to a second primer extension reaction utilizing a second polynucleotide synthesis primer capable of initiating said second reaction by hybridizing to a nucleotide sequence conserved among said compliments, thereby producing a plurality of different V_H-coding DNA homologs; and

(b) operatively linking to an expression vector for expression under the control of a promoter each of a plurality of said different V_H-coding DNA homologs.

3. The method of Claim 1 wherein said V_H-coding genes are V_H-coding DNA homologs and said isolating comprises:

(a) subjecting a complement of a V_H-coding gene repertoire to a primer extension reaction utilizing a polynucleotide synthesis primer capable of inhibiting said primer extension reaction by hybridizing to a nucleotide sequence conserved among said compliments, thereby producing a plurality of different V_H-coding DNA homologs; and

(b) operatively linking to an expression vector for expression under the control of a promoter each of a plurality of said different V_H-coding DNA homologs.

4. The method of Claim 1 wherein said V_L-coding

genes are V_L-coding DNA homologs and said isolating comprises:

(a) subjecting a V_L-coding gene repertoire to a first primer extension reaction utilizing a first polynucleotide synthesis primer capable of initiating said first reaction by hybridizing to a nucleotide sequence conserved with said repertoire, thereby producing a plurality of different V_L-coding DNA homolog complements, and subjecting said compliments to a second primer extension reaction utilizing a second polynucleotide synthesis primer capable of initiating said second reaction by hybridizing to a nucleotide sequence conserved among said compliments, thereby producing a plurality of different V_L-coding DNA homologs; and

(b) operatively linking to an expression vector for expression under the control of a promoter each of a plurality of said different V_L-coding DNA homologs.

5. The method of Claim 1 wherein said $_{VL\text{-coding}}$ genes are V_L-coding DNA homologs and said isolating comprises:

(a) subjecting a complement of a V_L-coding gene repertoire to a primer extension reaction utilizing a polynucleotide synthesis primer capable of inhibiting said primer extension reaction by hybridizing to a nucleotide sequence conserved among said compliments, thereby producing a plurality of different V_L-coding DNA homologs; and

(b) operatively linking to an expression vector for expression under the control of a promoter each of a plurality of said different V_L-coding DNA homologs.

6. The method of Claim 2 wherein said V_L-coding genes are V_L-coding DNA homologs and said isolating comprises:

(a) subjecting a V_L-coding gene repertoire to a third primer extension reaction utilizing a third polynucleotide synthesis primer capable of initiating said

third reaction by hybridizing to a nucleotide sequence conserved with said repertoire, thereby producing a plurality of different V_L-coding DNA homolog complements, and subjecting said compliments to a fourth primer extension reaction utilizing a fourth polynucleotide synthesis primer capable of initiating said fourth reaction by hybridizing to a nucleotide sequence conserved among said compliments, thereby producing a plurality of different V_L-coding DNA homologs; and

(b) operatively linking to an expression vector for expression under the control of a promoter each of a plurality of said different V_L-coding DNA homologs.

7. The method of Claim 2 wherein said V_L-coding genes are V_L-coding DNA homologs and said isolating comprises:

(a) subjecting a complement of a V_L-coding gene repertoire to a primer extension reaction utilizing a third polynucleotide synthesis primer capable of inhibiting said third primer extension reaction by hybridizing to a nucleotide sequence conserved among said compliments, thereby producing a plurality of different V_L-coding DNA homologs; and

(b) operatively linking to an expression vector for expression under the control of a promoter each of a plurality of said different V_L-coding DNA homologs.

8. A cloning system comprising first and second linear double stranded DNA vectors admixed in an aqueous medium together with an endonuclease, each of said vectors defining a promoter, a restriction site cleavable by said endonuclease, and a polylinker, said restriction site being located between said promoter and said polylinker on said first vector, said polylinker being located between said promoter and said restriction site on said second vector, said restriction site being cleavable to produce from each of said vectors respective first and second polylinker-

containing restriction fragments having termini complementary to one another.

9. A method of producing a linear double stranded DNA expression vector containing a 5' terminal promoter controlling the expression of V_L and V_H polypeptides from respective V_L- and V_H-coding genes, said V_L and V_H polypeptides being capable of forming a heterodimeric receptor of predetermined specificity, which method comprises:

(a) isolating a first diverse population of V_L-coding genes containing a gene coding for said V_L polypeptide, said first population being constituted by linear double stranded DNA molecules defining a restriction site recognized by an endonuclease, said restriction site located 5' terminal to said genes but 3' terminal to a promoter controlling the expression of said genes;

(b) isolating a second diverse population of V_H-coding genes containing a gene coding for said V_H polypeptide, said second population being constituted by linear double stranded DNA molecules defining said restriction site, said restriction site located 3' terminal to said V_H-coding genes, said V_H-coding genes located 3' terminal to a promoter controlling the expression of said V_H-coding genes;

(c) cleaving said double stranded DNA molecules while present in said populations with said endonuclease to produce restriction fragments having a cohesive terminus and either one of said V_L-coding genes or one of said V_H-coding genes; and

(d) randomly ligating said restriction fragments one to another via said cohesive terminus of each to produce a diverse population of double stranded linear DNA expression vectors having one of said V_H-coding genes and one of said V_L-coding genes in tandem on the same DNA strand and under the control of a single promoter;

(e) isolating from said diverse population of double stranded DNA expression vectors a vector capable of expressing said heterodimeric receptor of predetermined specificity.

10. The method of Claim 9 wherein said V_L-coding genes are V_H-coding DNA homologs and said isolating comprises:

(a) subjecting a V_H-coding gene repertoire to a first primer extension reaction utilizing a first polynucleotide synthesis primer capable of initiating said first reaction by hybridizing to a nucleotide sequence conserved with said repertoire, thereby producing a plurality of different V_H-coding DNA homolog complements, and subjecting said compliments to a second primer extension reaction utilizing a second polynucleotide synthesis primer capable of initiating said second reaction by hybridizing to a nucleotide sequence conserved among said compliments, thereby producing a plurality of different V_H-coding DNA homologs; and

(b) operatively linking to an expression vector for expression under the control of a promoter each of a plurality of said different V_H-coding DNA homologs.

11. The method of Claim 9 wherein said V_H-coding genes are V_H-coding DNA homologs and said isolating comprises:

(a) subjecting a complement of a V_H-coding gene repertoire to a primer extension reaction utilizing a polynucleotide synthesis primer capable of inhibiting said primer extension reaction by hybridizing to a nucleotide sequence conserved among said compliments, thereby producing a plurality of different V_H-coding DNA homologs; and

(b) operatively linking to an expression vector for expression under the control of a promoter each of a plurality of said different V_H-coding DNA homologs.

12. The method of Claim 9 wherein said V_L-coding

genes are V_L-coding DNA homologs and said isolating comprises:

(a) subjecting a V_L-coding gene repertoire to a first primer extension reaction utilizing a first polynucleotide synthesis primer capable of initiating said first reaction by hybridizing to a nucleotide sequence conserved with said repertoire, thereby producing a plurality of different V_L-coding DNA homolog complements, and subjecting said compliments to a second primer extension reaction utilizing a second polynucleotide synthesis primer capable of initiating said second reaction by hybridizing to a nucleotide sequence conserved among said compliments, thereby producing a plurality of different V_L-coding DNA homologs; and

(b) operatively linking to an expression vector for expression under the control of a promoter each of a plurality of said different V_L-coding DNA homologs.

13. The method of Claim 9 wherein said V_L-coding genes are V_L-coding DNA homologs and said isolating comprises:

(a) subjecting a complement of a V_L-coding gene repertoire to a primer extension reaction utilizing a polynucleotide synthesis primer capable of inhibiting said primer extension reaction by hybridizing to a nucleotide sequence conserved among said compliments, thereby producing a plurality of different V_L-coding DNA homologs; and

(b) operatively linking to an expression vector for expression under the control of a promoter each of a plurality of said different V_L-coding DNA homologs.

14. The method of Claim 10 wherein said V_H-coding genes are V_L-coding DNA homologs and said isolating comprises:

(a) subjecting a V_L-coding gene repertoire to a third primer extension reaction utilizing a third polynucleotide synthesis primer capable of initiating said

third reaction by hybridizing to a nucleotide sequence conserved with said repertoire, thereby producing a plurality of different V_L-coding DNA homolog complements, and subjecting said compliments to a fourth primer extension reaction utilizing a fourth polynucleotide synthesis primer capable of initiating said fourth reaction by hybridizing to a nucleotide sequence conserved among said compliments, thereby producing a plurality of different V_L-coding DNA homologs; and

(b) operatively linking to an expression vector for expression under the control of a promoter each of a plurality of said different V_L-coding DNA homologs.

15. The method of Claim 10 wherein said V_L-coding genes are V_L-coding DNA homologs and said isolating comprises:

(a) subjecting a complement of a V_L-coding gene repertoire to a primer extension reaction utilizing a third polynucleotide synthesis primer capable of inhibiting said third primer extension reaction by hybridizing to a nucleotide sequence conserved among said compliments, thereby producing a plurality of different V_L-coding DNA homologs; and

(b) operatively linking to an expression vector for expression under the control of a promoter each of a plurality of said different V_L-coding DNA homologs.

add a2) add c1)